AMENDMENTS TO THE SPECIFICATION

The paragraph beginning at page 15, line 30, has been amended as follows:

Thus, in a preferred method of the invention the PBMCs are allowed or induced to proliferate prior to step (b). The PBMCs are allowed to proliferate at least one cell cycle. Preferably the PBMCs are allowed or induced to proliferate in the presence of a proliferating agent. Preferred proliferating agents include *e.g.* anti-CD3/anti-CD28 antibodies, IL-2, PHA, ConA, GM-CSF and IL-4.In a further preferred method of the invention the mononuclear cells are enriched for a subfraction of mononuclear cells subsequent to step (b), *i.e.,* subsequent to the introduction of the IL-10 transgene. Enrichment for specific subfractions of mononuclear cells may be performed as described above for the enrichment prior to step (b). In addition, the enrichment subsequent to step (b) may include the enrichment for cells (over)expressing the IL-10 transgene. Enrichment for cells (over)expressing the IL-10 transgene may be performed by direct sorting or screening for cells expressing IL-10, using *e.g.* labelled anti-IL-10 antibodies. However, most conveniently cells (over)expressing the IL-10 transgene are selected using an expression construct comprising a second nucleotide sequence coding for a marker protein as described above. Cells (over)expressing the IL-10 transgene may then be sorted using a fluorescently labelled marker protein such GFP or one of its variants or by using an antibody. Alternatively, cells (over)expressing the IL-10 transgene may be selected for by growth in a selective medium allowing only growth of cells expressing a selectable marker gene such as described above. Thus, in a preferred method of the invention the mononuclear cells are enriched subsequent to step (b) for cells (over)expressing the IL-10 transgene. Whether or not it is necessary to culture the PBMCs prior to step (b) depends on both the type of vector that is used for the introduction of the IL-10 transgene (*e.g.* MMLV- and Lenti viral-based vectors are capable of infection non-dividing cells whereas most other viral vectors are not), and on the type of mononuclear cell to be used (*e.g.* PBMCs may be enriched for dendritic cells (DCs) by culturing monocytes, isolated from PBMCs, with IL-4 and GM-CSF, as described above).

Paragraph beginning at page 16, line 24, has been amended as follows:

A particularly preferred method relates to the production of T cells that are transgenic for IL-10 and that functionally behave as regulatory T cells in that they express IL-10 and have anti-inflammatory and immunosuppressive functions. This method comprises the steps of: (a) optionally, culturing PBMCs in the presence of a proliferating agent such as phytohemagglutinin (PHA), or αCD3/CD28 and/or IL-2 (preculturing of the PBMCs is not necessary when MMLV or lenti viral vectors are used for the introduction of the IL-10 transgene in step (b)); (b) introducing an IL-10 expression construct as described above; (c) optionally, sorting the T cells or selecting cells expressing the IL-10 transgene; and (d) optionally, expanding the cells in the presence of a feeder mixture consisting of irradiated PBMCs, irradiated JY cells, anti-CD3/anti-CD28 antibodies, PHA

and/or IL-2. The thus obtained transgenic regulatory T cells are characterised by their biological activity as evidenced by decreased proliferation of autologous responder cells and decreased production of the pro-inflammatory cytokine IL-12 by dendritic cells in co-culture experiments.

Paragraph beginning at page 29, line 28 has been amended as follows:

1.2.1 Efficient transduction and sorting of murine splenocytes

To generate IL-10 expressing $CD4^+$ cells, activated murine splenocytes were transduced with the IL-10-GFP retroviral construct. αCD3/CD28 mAb-activated splenocytes routinely consisted of 42±5% $CD4^+$ cells. The percentage of GFP-expressing cells (transduction efficiency) in several independent experiments (n=11) was 16±2%. After 48 hours, viable GFP^+CD4^+-expressing splenocytes were sorted using a FACS Vantage flow cytometer (Figure 1), while GFP^-CD4^+ cells served as negative controls, resulting in populations of 89±2% (GFP^+CD4^+ cells) and 97±1% (GFP^- $CD4^+$ cells), respectively.

Paragraph beginning at page 39, line 2, has been amended as follows

As previously reported, transgene expression increases substantially when retroviral transduced lymphocytes are reactivated by CD3/CD28 engagement.[57] IL-10-GFP $CD4^+$ cells up-regulated IL-10 expression indeed after αCD3/CD28 stimulation significantly compared to resting cells. A representative example is given in Figures 11A and 11B. These results were highly reproducible when studied in 8 other donors: stimulated IL-10 production was 12.9 ± 2.1 (Figure 12) versus 0.59 ± 0.06 ng/ml/48 h by resting IL-10-GFP $CD4^+$ cells (p=0.003). [[A]]αCD3/CD28 stimulation of control GFP $CD4^+$ cells also led to a higher IL-10 expression (Figure 12) compared to non-stimulated $CD4^+$ cells (2.08 ± 0.61 versus 0.19 ± 0.1 ng/ml/48 h, p=0.002), though these levels were evidently lower than the IL-10 levels in the supernatants of the IL-10-GFP $CD4^+$ cells.